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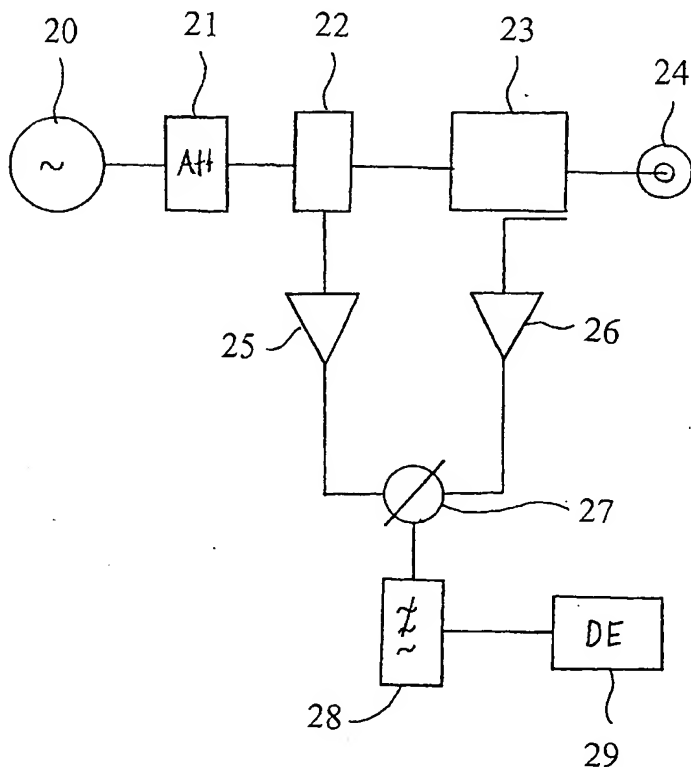
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[Continued on next page]

(54) Title: **METHOD FOR MEASURING OF EDEMA**



(57) Abstract: The invention relates to a method for measuring tissue edema. By a method in accordance with the invention an electromagnetic probe (24) is placed on the skin, and the capacitance of the probe is proportional to the dielectric constant of the skin and subcutaneous fat, which is proportional to the water content of the skin. The edema is scored by measuring the capacitance of the electromagnetic probe, so called open-ended coaxial cable, at a high frequency, approximately 20-500 MHz.

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

METHOD FOR MEASURING OF EDEMA

The present invention relates to a method for measuring tissue edema.

Edema in biological material is a state where more water is accumulated in the tissue than in a normal physiological situation. An accumulation of extra water in soft organs leads to an increase in volume. Water in tissue is either intracellular or extracellular. It is carried to the tissue in the blood, the plasma in the blood is continually exchanging with the water in the tissue.

Edema develops if more water is imported to tissue than exported from it. The reason for edema may be a constriction or a thrombus in the vein transporting the blood from the tissue, the increased permeability of plasma from the blood vessels, inflammation of the tissue or dilation of vessels caused by an internal or external reason. Edema is always a serious symptom of a disturbance in blood circulation, increased permeability of vessels or inflammations. Therefore the measurement of edema is of great medical significance.

Edema in limbs is usually measured by using a tape measure. US-patent publication 5,891,059 describes a method where limb edema is detected by measuring the circumference of the limb and comparing the result against a control value. The difference between the readings describes the value of edema in the patient. The increase of circumference describes then the general limb edema, but does not give knowledge of the edema in difference tissue formations. The increase in tissue volume caused by edema can be detected by medical imaging devices such as computer tomography or MRI. However, these methods are expensive.

Edema can also be measured by weighting the body mass. It can also be followed up by fluid balance calculation where all the liquids taken internally are measured and compared with natural liquid losses.

The most common way to assess skin edema is to press the skin by hand for a while and then to check how much it takes for the skin to even-out again. For normal skin it takes a few seconds but for swollen skin it may take even tens of seconds. US-patent publication 5,957,867 describes a method where the limb is set on a plate where a moveable rod is connected. The rod is pushed through a hole in the plate onto the skin surface and is then pushed further to a predefined distance. At the same time a system attached to the device measures the pressure profile, which is proportional to the rate of edema. Obviously these methods are not accurate nor give any specific knowledge of the tissue.

According to well-known techniques the dielectric constant of biological tissues has been measured with electrodes placed inside the tissue. The benefit of these methods is the close contact of the electrodes with the target volume. The measurement is made by sending an oscillating electromagnetic field into the tissue.
5 ~~From the interaction of the electric field and the tissue the dielectric properties of~~
the tissue can be calculated as a function of frequency. The result of the dielectric measurement is usually a value measured by one or more frequencies. It is proportional to the complex permittivity, dielectric constant or conductivity of the tissue. The disadvantage of these techniques is that the electrodes, usually 2-4, have
10 to be placed invasively into the tissue, hence damaging the tissue.

These kinds of methods are used to measure the dielectric properties of tissues, which are proportional to the water content. When the water content of tissue is changing within the normal limits it is not an edema e.g. increased water content, but normal physiological functioning.

15 US-patent publication 5,580,727,0 describes an electric measuring device for brain edema, by which the intracellular edema in brain cells can be monitored for hours or days. The device is electrically insulated from the mains voltage and feeds an AC current of 1mA at a frequency of 200 Hz to the outer electrodes of a four-electrode system on the skin surface. The middle electrodes are located inside the skull. The
20 disadvantage of this method is the surgery required.

The object of the present invention is to provide a method, which obviates the shortcomings of the present systems. Furthermore the object of the invention is to provide an advantageous method for measuring a local tissue edema from the skin surface of person non-invasively and continuously or instantly. It is a further
25 objective to provide a method, which does not impose any restrictions on the measurement site or the type of edema.

The object of the invention is achieved by the method, which is described in the claims.

30 In a method in accordance with the invention an electromagnetic probe is placed in contact with the skin, in which case the capacitance of the probe is proportional to the dielectric constant of the underlying tissue, which is further proportional to the water content of skin, and the edema is scored by measuring the capacitance of the probe at a high frequency, approximately 20-500 MHz. The probe is an open-ended coaxial cable.

In the method a coaxial electrode is placed on the skin, and an electromagnetic field, with a high frequency (20-500 MHz), is transmitted through the skin and subcutaneous fat tissue. The field that is reflected back from the tissue is measured. From the reflected field the dielectric constant of the skin can be calculated. The dielectric constant is proportional to the relative water content of the skin, which increases as the edema develops. The measured value is partly affected by the dielectric constant of the subcutaneous fat tissue, which is low because of its low water content. The skin becomes thicker as the edema increases and the fat tissue moves further from the probe with the result that its effect is decreased. Therefore the two effects of the edema, the increased dielectric constant of skin and the thickening of the skin change the measured value in the same direction.

An essential feature of the invention is the high radio frequency (approximately 20-500 MHz), because at these frequencies the electric field penetrates deeply into the skin and subcutaneous fat tissue. At lower frequencies the electric field is concentrated on the superficial layers of the skin and the measurement of edema is not possible.

Substantial benefits are obtained with the present invention. Edema can be monitored locally from the surface of the skin by placing the electrode on the measuring site for a long time. Edema can be monitored without any invasive operation of a part of the measuring device. Measurements taken by the device according the invention do not disturb the edema in any way. With the invention the assessment of the effect of medical proceedings, liquid treatments, medication and physical treatments on the edema can be improved.

In an advantageous application of the invention the measurement is made manually with only a few seconds measurement. In this way a local edema can be rapidly detected. In another advantageous application of the invention the measurement is made by placing the probe on the skin for a long time, for instance hours or days, with an attachment, such as a strap. In this way the edema can be monitored continuously for a long time.

In a further advantageous application of the invention the device operates only at one exactly pre-selected frequency. The electrical properties of a tissue are dependent on the frequency and therefore reliable and comparable information from the tissue can be obtained by measuring with only one pre-selected frequency.

In a further advantageous application of the invention the edema is measured from the upper layers of the skin by using 20-50 MHz radio frequencies, in which case the electric field is concentrated on these layers. In this way the upper layers of the skin can be measured without any delay and reliably.

- 5 In a further advantageous application of the invention the edema is measured from deeper layers of the skin by using 50-500 MHz radio frequencies, in which case the electric field penetrates deeply into the skin tissue (dermis) and the underlying subcutaneous fat tissue. In this way the deeper layers of the skin and the underlying fat tissue can be measured without any delay and reliably.
- 10 The invention will now be described in greater detail with reference to the accompanying drawings, where

Fig. 1 shows a block diagram showing the operation of the device,

Fig. 2 shows the probe connected to the electronic unit by a coaxial cable,

- Fig. 3 shows the result of an example case of developing edema in pig skin caused by controlling blood circulation at sites A and B. Sites C and D are the controls.
- 15

Figure 1 shows an probe including an oscillator 20, an attenuator 21, a power splitter 22, a directional coupler 23, a probe 24, amplifiers 25 and 26, a phase detector 27, a low pass filter 28 and a digital electronic unit 29. The block diagram in Fig. 1 can vary in different applications of the method. It may also be utilised in other ways.

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Figure 2 shows the probe 24, including an inner electrode 30, a Teflon insulator 31, an outer electrode 32, a coaxial cable 33 and an electronic unit 34 comprising the components of Fig. 1 excluding the probe 24.

- An essential feature of the device according to the invention is that the coaxial probe is large enough, in order for the electric field to penetrate up to the subcutaneous fat tissue. The distance between the two electrodes of the probe should be about 2-10 mm.
- 25

The device operates so that the sinusoidal high frequency (20-500 MHz) signal from the oscillator 20 is led through the attenuator 21, power splitter 22 and directional coupler 23 to the probe 24. The signal is reflected back from the probe. Part of this reflected signal is led through the directional coupler 23 to the amplifier 26 and further to one input of the phase detector 27. The signal coming straight

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from the oscillator 20 is led through the power splitter 22 to the other input of the phase detector 27. The output from the phase detector is led to the low pass filter 28, whose output is a DC voltage proportional to the capacitance of the probe 24. This voltage is further led to the digital electronic unit, where it is AD-converted,
5 scaled and recorded.

The output of the phase detector 27 after the low pass filtering is proportional to the phase difference, which is only dependent on the capacitance of the probe 24. The device operates on a single precisely set frequency and therefore the result is only dependent on the dielectric properties of the tissue and not on the conductivity.

- 10 The probe 24 is connected to the directional coupler 23 via the coaxial cable so that the signal is connected to the inner conductor of the cable and further to the inner electrode 30 of the probe 24, and the ground signal is connected to the outer conductor of the cable and further to the outer electrode 32 of the probe 24.

Fig. 1 shows only one example of the high frequency implementation of the
15 method. It is made using known techniques. The essential feature is that the capacitance of the probe is measured at a high frequency 20-500 MHz.

The high frequency unit of the device, comprising of parts 20-27, is realised using standard radio techniques. In practice this means that the components are connected to each other with microstrip lines which have a defined impedance, for instance 50
20 ohms. Therefore the same signal line can propagate signals in both directions simultaneously. The fact that the dimensions of the circuit are small compared to the wavelength does not in any way affect the operation of the high frequency components.

An essential feature of the high frequency unit is that the signal amplitude in both
25 inputs of the phase detector 27 is so high that the detector operates in a saturated state. Therefore the phase detector 27 measures only the phase difference of the incoming signals. This phase difference is proportional to the capacitance of the probe 24 and further proportional to the dielectric constant of the tissue. The dielectric constant is dependent on the water content of the skin.

30 Another essential feature of the high frequency unit is the attenuator 21 between the oscillator 20 and the power splitter 22. Its purpose is to prevent the access of the signal reflected from the probe to the amplifier 25. Under the influence of the amplifier the signal reflected from the probe goes twice through the attenuator 21 when propagating to the input of the amplifier 25. Therefore, if the attenuation of

the attenuator 21 is for instance 6 dB, the total attenuation of this signal is 12 dB, which is adequate.

- Fig. 3 shows as an example case of a measurement of a developing edema in pig skin, where by controlling the blood circulation a local edema is caused at sites A and B. Sites C and D are the controls. It can be seen that at the sites with edema (A and B) the dielectric constant is increased by over 40 % compared to the baseline. At the control area (sites C and D) where the developing edema does not exist the measured values remain unchanged. The measurement reacts rapidly to the edema, even before it is noticeable for instance by finger pressure.
- 10 The present invention is not restricted to the aforementioned advantageous application, but can be utilised in other forms within the limits of the idea of the invention as defined by the claims.

CLAIMS

1. A method for measuring tissue edema, *characterised* by
 - an electromagnetic probe (24) is placed on the skin during the measurement, and the capacitance of the probe is proportional to the dielectric constant of the skin and the subcutaneous fat tissue, which is further proportional to the water content of the skin, and that
 - the edema is scored by measuring the capacitance of the electromagnetic probe, so called open-ended coaxial cable, at a high frequency, approximately 20-500 MHz.
2. A method according to claim 1, *characterised* in that the measurement is made manually and takes only a few seconds.
3. A method according to claim 1, *characterised* in that for the measurement the probe is secured on the skin by an attachment, such as strap-like attachment, for a long time, for instance hours or days, in which case the edema can be monitored continuously.
4. A method according to any of the claims 1-3, *characterised* in that the device operates only on a single precisely set frequency.
5. A method according to any of the claims 1-4, *characterised* in that edema of the uppermost layers of the skin is measured using a frequency of approximately 20-50 MHz, in which case the electric field is concentrated in the uppermost layers of the skin.
6. A method according to any of the claims 1-4, *characterised* in that the edema of deep skin layers and the underlying subcutaneous fat is measured using a frequency of approximately 50-500 MHz, in which case the electric field penetrates deeply into the skin and the underlying subcutaneous fat.

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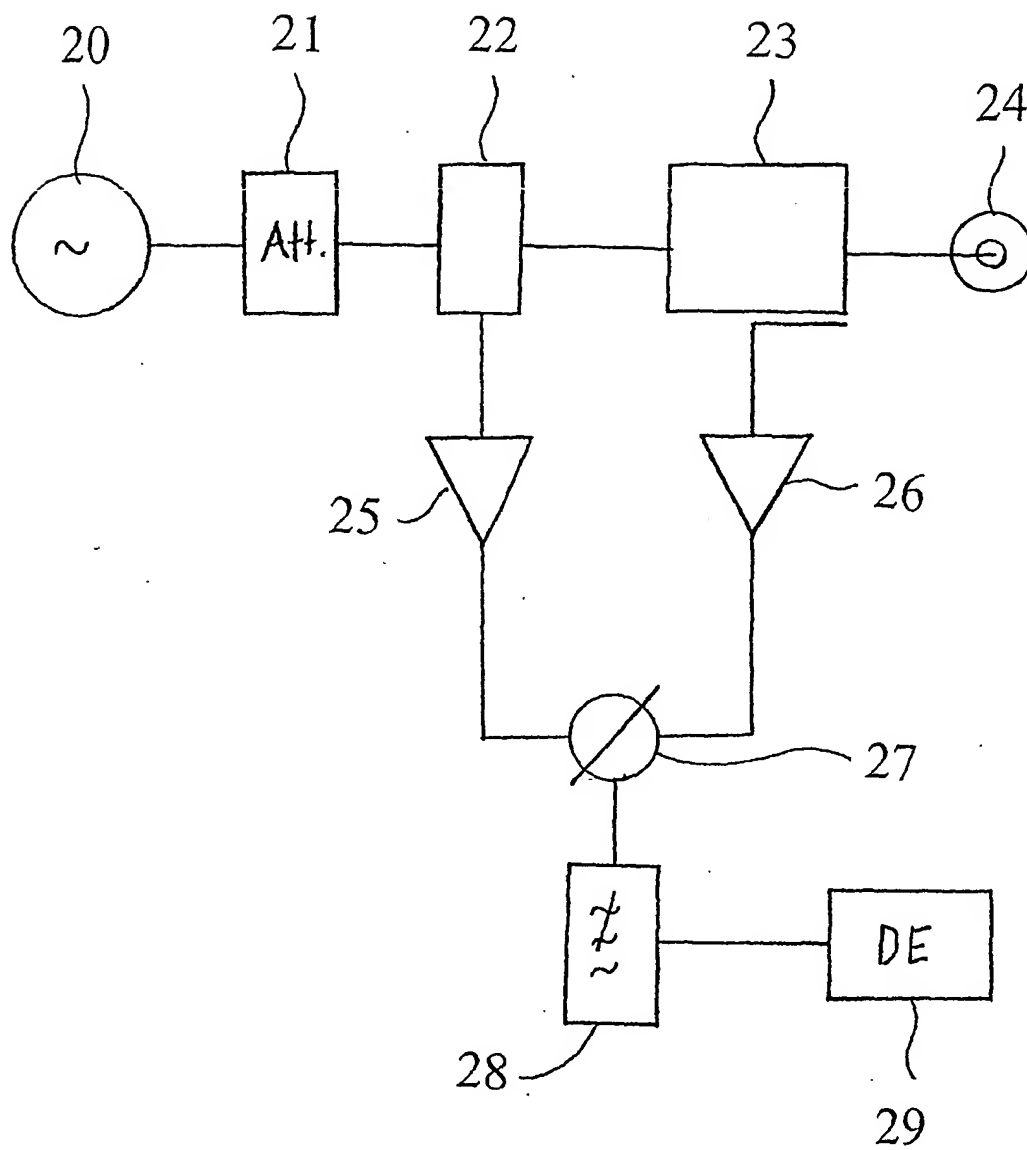


FIG. 1

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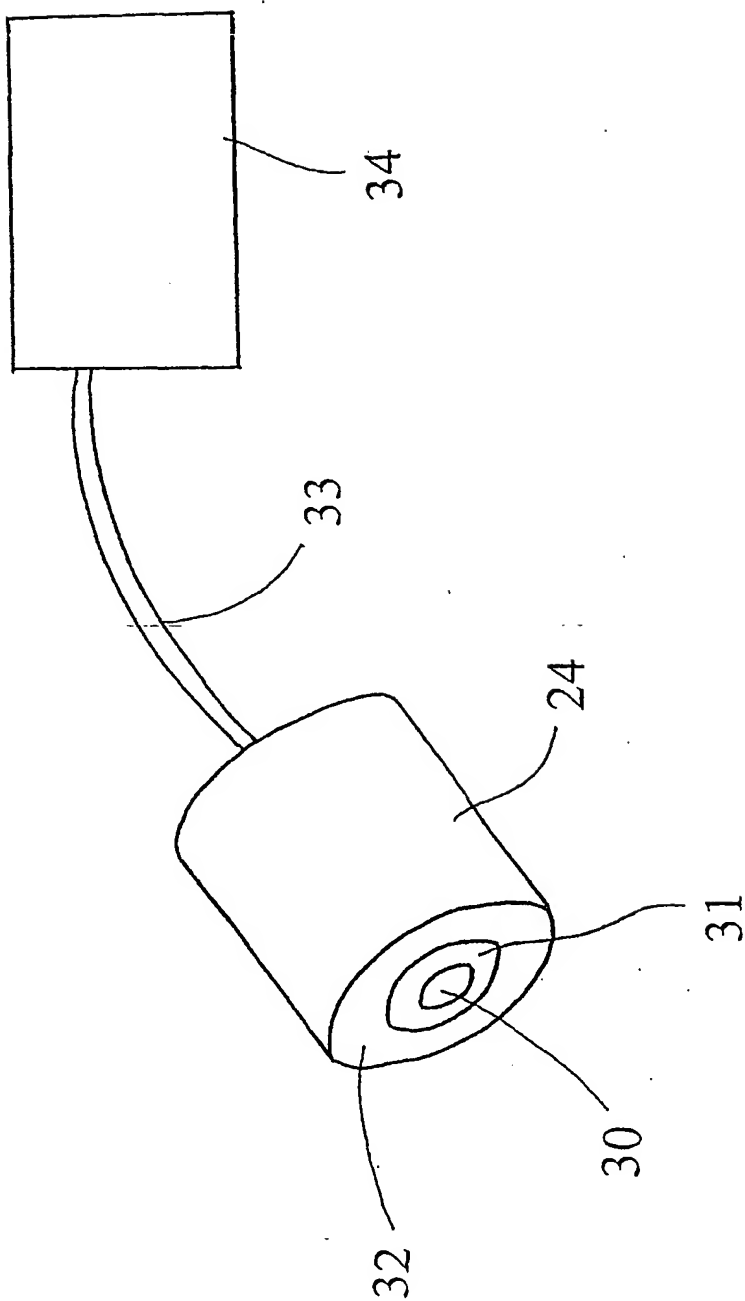


FIG. 2

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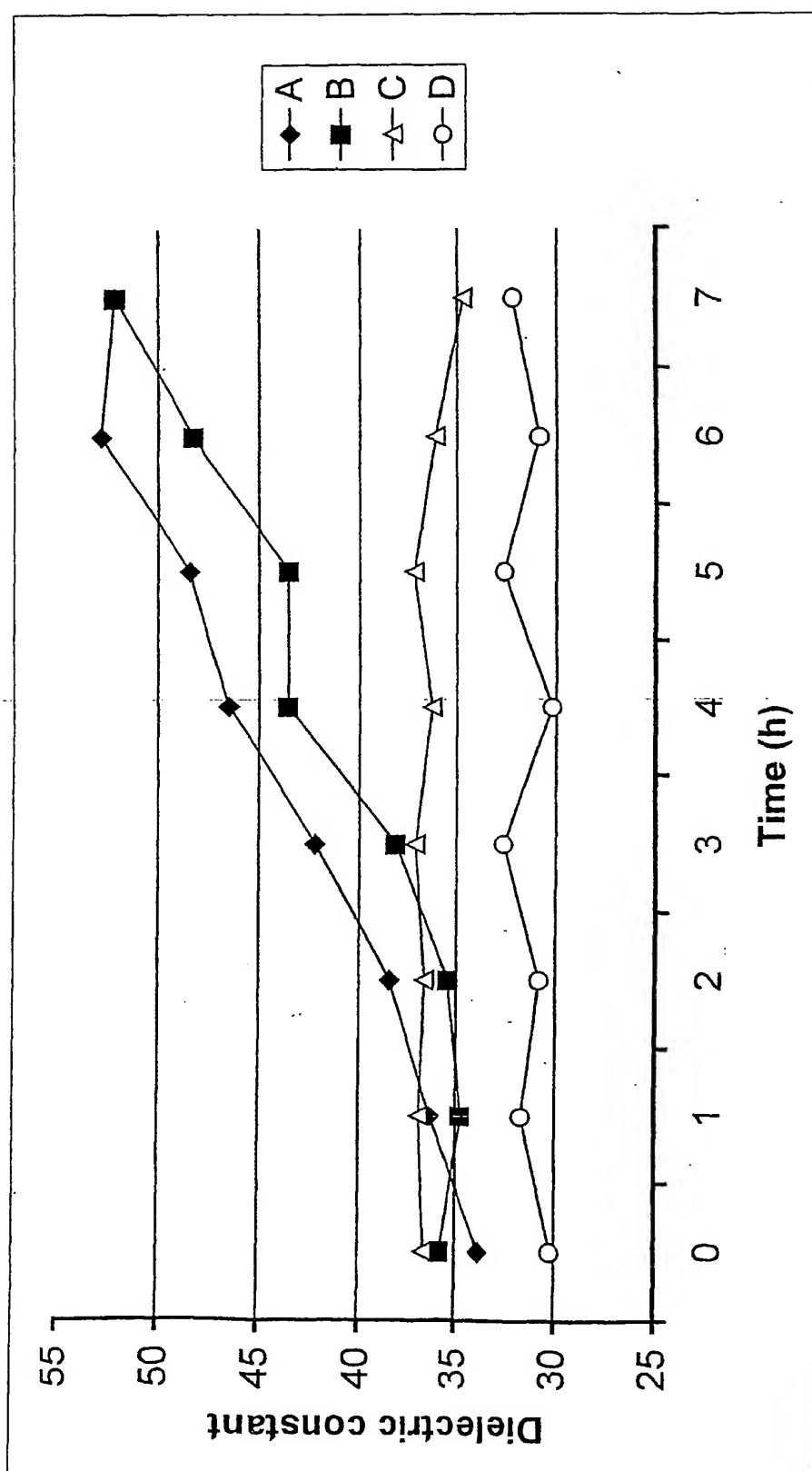


FIG. 3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/FI 02/00234

A. CLASSIFICATION OF SUBJECT MATTER

IPC7: A61B 5/053

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: A61B, G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-INTERNAL, WPI DATA, PAJ, INSPEC, MEDLINE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING, Volume 46, No 9, Sept 1999, H. Pin Kao et al., "Correlation of Permittivity and Water Content During Cerebral Edema", page 1121 - page 1128, see especially "introduction", last paragraph --	
A	WO 0079255 A1 (THE UNIVERSITY OF QUEENSLAND ET AL.), 28 December 2000 (28.12.00), claim 17 -----	

☐ Further documents are listed in the continuation of Box C.☒ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

1 August 2002

Date of mailing of the international search report

05 -08- 2002

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06/07/02

PCT/FI 02/00234

Form PCT/ISA/210 (patent family annex) (July 1998)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/FI02/00234

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: **1-6**
because they relate to subject matter not required to be searched by this Authority, namely:
see next sheet.
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/FI02/00234

Claims 1-6 relate to a diagnostic method. Thus the International Search Authority is not required to carry out an international search for these claims (Rule 39.1(iv)). Nevertheless, a search has been executed for the apparatus described in claim 1.